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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/582,304	KIMURA ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,16 and 22-28* is/are rejected.

7)☒ Claim(s) *8-15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/31/07, 10/4/07, 2/12/08, 6/11/08, 9/13/08, 1/20/09, 2/9/09, 2/24/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-7 and 22-28, in the reply filed on December 16, 2008 is acknowledged. The traversal is on the ground(s) that unity of invention is not lacking because the Ozaki, et al. reference does not anticipate the claims and that searching all of the claims would not be an undue burden on the examiner (see arguments pages 1-3, December 16, 2008). This is not found persuasive because although the Ozaki, et al. reference does not anticipate the claims as demonstrated by applicant, claim 1 is obvious over Ozaki, et al. in view of Kortt, et al. as set forth below (see 103a rejection). Therefore there is no special technical feature linking the groups. Regarding the search burden on the examiner, national stage entry of PCT cases are not restricted based on search burden, rather the restriction is based on lack of unity and a special technical feature shared by the groups. "Examiners are reminded that unity of invention (not restriction practice pursuant to 37 CFR 1.141 - 1.146) is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. 371." See MPEP 1893.03(d).

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 16, 2008.

3. Claims 1-16 and 22-28 are under examination.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on May 31, 2007, October 4, 2007, February 12, 2008, June 11, 2008, September 13, 2008, January 20, 2009, February 9, 2009, February 24, 2009, and March 27, 2009 have been considered by the examiner and an initialed copy of the IDS is included with the mailing of this office action.

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

6. The disclosure is objected to because of the following informalities: the specification contains sequences on pages 8 and 20 which are not identified by SEQ ID No. and do not appear to be included in the sequence listing. See 37 CFR §1.821-1.825

Appropriate correction is required.

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Antibodies that bind HLA-A for inducing cell death.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to an sc(Fv)2 comprising an amino acid sequence with one or more amino acid substitutions, deletions, additions, and/or insertions in the amino acid sequence of any one of claims 8 to 15, wherein the sc(Fv)2 also has an activity equivalent to that of the antibody of any one of claims 8 to 15.

The specification discloses that SEQ ID No. 10 is the sequence of the heavy chain variable domain and SEQ ID No. 12 is the sequence of the light chain variable

domain. The specification discloses that SEQ ID No. SEQ ID No. 14 is an scFv sequence and SEQ ID No. 2 is the sc(Fv)2 sequence.

The specification does not provide sufficient written description as to the structural features of the claimed genus of sc(Fv)2 molecules and the correlation between the chemical structure and function of the genus of sc(Fv)2 molecules. The specification does not disclose a single species with less than 100% sequence identity with the sequences of SEQ ID Nos. 10, 12, 14, and 2.

A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir.

2004)(Claims directed to PTFE dental floss with a friction-enhancing coating were not supported by a disclosure of a microcrystalline wax coating where there was no evidence in the disclosure or anywhere else in the record showing applicant conveyed that any other coating was suitable for a PTFE dental floss.).

It has been well known that minor structural differences even among structurally related compounds can result in substantially different biology, expression and activities. Based on the instant disclosure one of skill in the art would not know which sequences are essential, which sequences are non-essential and what particular sequence lengths identify essential residues for identifying an sc(Fv)2 encompassed by the claimed specificity. For example, there is insufficient guidance based on the reliance of disclosure of SEQ ID Nos. 10, 12, 14, and 2 to direct a person of skill in the art to select or to predict particular residues as essential for identifying variants of the sequences that would bind HLA. Mere idea of function is insufficient for written description; isolation and characterization at a minimum are required.

Skolnick et al (Trends in Biotechnology, 2000. Vol. 18, pages 34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based on sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to function of the structurally related protein (see in particular "Abstract" and Box 2).

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology, 1990. Vol. 111, pages 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology, 1988. Vol. 8, pages 1247-1252).

In the absence of sufficient guidance and direction to the structural and functional analysis, applicant's reliance on the activity of the antibody encoded by SEQ ID Nos. 14 and 2 disclosed in the specification as-filed does not appear to provide sufficient written description for the genus of antibodies encompassed by the claimed genus in view of the above evidence, which indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed.

For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case, applicant has not even disclosed a single species encompassed by the highly variant genus nor is there disclosure of the common attributes or features (i.e., structural domains) that are essential for activity or those which are non-essential. See, e.g., Eli Lilly. Description of a representative number of species does not require the description to be of such specificity that it would

provide individual support for each species that the genus embraces. If a representative number of adequately described species are not disclosed for a genus, the claim to that genus must be rejected as lacking adequate written description under 35 U.S.C. 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddles v.Baird*, 30 USPQ2d 1481, 1483. In *Fiddles v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only the antibodies of SEQ ID Nos. 10, 12, 14, and 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

10. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies comprising the CDRs of SEQ ID Nos. 3-8, or the heavy chain of SEQ ID No. 10 and the light chain of SEQ ID No. 12, or the scfv of SEQ ID No. 14 or the sc(Fv)2 of SEQ ID No. 2, does not reasonably provide enablement for amino acid sequences with one or more amino acid substitutions, deletions, additions and/or insertions in the amino acid sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claim is broadly drawn to an sc(Fv)2 comprising an amino acid sequence with one or more amino acid substitutions, deletions, additions, and/or insertions in the amino acid sequence of any one of claims 8 to 15, wherein the sc(Fv)2 also has an activity equivalent to that of the antibody of any one of claims 8 to 15.

The specification discloses that SEQ ID No. 10 is the sequence of the heavy chain variable domain and SEQ ID No. 12 is the sequence of the light chain variable domain. The specification discloses that SEQ ID No. SEQ ID No. 14 is an scFv sequence and SEQ ID No. 2 is the sc(Fv)2 sequence. The specification does not describe any variations in the sequences.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin (Schwartz et al, Proceedings of the National Academy of Sciences, 1987. Vol. 84, pages 6408-6411). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin et al, Biochemistry, 1975. Vol. 14, pages 1559-1563).

Specifically related to antibodies, it is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of

the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proceedings of the National Academy of Sciences, 1982. Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

The fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen binding site, is underscored by Casset et al. (Biochemical and Biophysical Research Communications, 2003. Vol. 307, pages 198-205) which constructed a peptide mimetic of an anti-CD4 monoclonal antibody binding site by rational design and the peptide was designed with 27 residues formed by residues from 5 CDRs (see entire document). Casset et al. also states that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, left column) and this is demonstrated in this work by using all CDRs except L2 and additionally using a framework residue located just before the H3 (see page 202, left column). Vajdos et al. (Journal of Molecular Biology, 2002.

Vol. 321, pages 415-428) additionally state that antigen binding is primarily mediated by the CDRs more highly conserved framework segments which connect the CDRs are mainly involved in supporting the CDR loop conformations and in some cases framework residues also contact antigen (page 416, left column). Holm et al (Molecular Immunology, 2007. Vol. 44, pages 1075-1084) describes the mapping of an anti-cytokeratin antibody where although residues in the CDR3 of the heavy chain were involved in antigen binding unexpectedly a residue in CDR2 of the light chain was also involved (abstract). Chen et al. (Journal of Molecular Biology, 1999. Vol. 293, pages 865-881) describe high affinity variant antibodies binding to VEGF wherein the results show that the antigen binding site is almost entirely composed of residues from heavy chain CDRs, CDR-H1, H2, H3 (page 866). Wu et al. (Journal of Molecular Biology, 1999. Vol. 294, pages 151-162) state that it is difficult to predict which framework residues serve a critical role in maintaining affinity and specificity due in part to the large conformational change in antibodies that accompany antigen binding (page 152 left column) but certain residues have been identified as important for maintaining conformation.

There is insufficient evidence or nexus that would lead the skilled artisan to predict the ability to produce an antibody that binds HLA and comprises one or more amino acid substitutions, deletions, additions and/or insertions in the amino acid sequence. The specification does not teach modifications of the antibody sequences.

In view of the lack of the predictability of the art to which the invention pertains undue experimentation would be required to produce the claimed antibodies with a

reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively produce the claimed antibodies and absent working examples providing evidence which is reasonably predictive that the claimed substitutions, deletions, additions and/or insertions are effective for binding HLA, commensurate in scope with the claimed invention.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.,* 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-7 and 22-28 are rejected under 35 U.S.C. 103(a) as being obvious over Ozaki, et al. (Blood, 2003. Vol. 102, page 933a, as cited on the IDS filed May 31, 2007) in view of Kortt, et al. (Biomolecular Engineering, 2001. Vol. 18, pages 97-108, as cited on the IDS filed May 31, 2007).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing

that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claims recite an antibody comprising two heavy chain variable regions and two light chain variable regions, wherein the antibody is a single chain polypeptide having a binding activity against human leukocyte antigen (HLA), wherein the two heavy chain variable regions and two light chain variable regions are arranged in the order of heavy chain variable region, light chain variable region, heavy chain variable region, and light chain variable region, starting from the N terminus of the single chain polypeptide, wherein the two heavy chain variable regions and two light chain variable regions are linked by a linker, wherein the linker comprises 15 amino acids, wherein HLA is HLA class I, wherein HLA class I is HLA-A, wherein the antibody is sc(Fv)2. A cell death-inducing agent comprising the antibody of claim 1 as an active ingredient, wherein the agent has cell death inducing activity against B cells or T cells, wherein the B cells or T cells are activated B cells or activated T cells. A cell growth inhibitory agent comprising the antibody of claim 1 as an active ingredient. An antitumor agent comprising the antibody of claim 1 any as an active ingredient, wherein the tumor is a blood tumor. A therapeutic agent for autoimmune diseases, wherein the agent comprises the antibody of claim 1 as an active ingredient.

Ozaki, et al. teach a recombinant scfv diabody which binds to HLA and has a cell death inducing function, a cell growth inhibitory function, and an anti myeloma (blood tumor) function. Ozaki, et al. do not teach an sc(Fv)2 antibody. This deficiency is made up for in the teachings of Kortt, et al.

Kortt, et al. teach how the length of the linker affects the formation of scfv multimers including sc(Fv)2 (see pages 96 1st column and figure 3). Kortt, et al. teach linkers for scFv molecules to be up to 15 amino acids long (figure 3).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody of Ozaki, et al. to produce an sc(Fv)2 which maintained the cell death inducing, cell growth inhibiting and anti myeloma functions in view of Kortt, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody of Ozaki, et al. to produce an sc(Fv)2 which maintained the cell death inducing, cell growth inhibiting and anti myeloma functions in view of Kortt, et al. because Kortt, et al. teach that scfv multimers (i.e. sc(Fv)2) are significantly larger than scfv monomers and thus have an advantage in *in vivo* application by minimizing the rapid first pass clearance rate of the molecule (page 103, 5. Size of di- and tri-abodies and effect on *in vivo* pharmacokinetics). Kortt, et al. also teach the advantage of multivalent scFvs over monovalent scfvs is the gain in functional binding affinity to target antigens. (page 104, 6. Avidity and flexibility in scfv multimers). Further, it is routine in the art to determine the sequence of a protein, therefore, one of ordinary skill in the art would have been able to determine the sequence of the Ozaki, et al. antibody to enable manipulation of the antibody into various forms including sc(Fv)2. Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody of

Ozaki, et al. to produce an sc(Fv)2 which maintained the cell death inducing, cell growth inhibiting and anti myeloma functions in view of Kortt, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

15. Claims 1-7, 16, and 22-28 are rejected.

Claims 8-15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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Anne M. Gussow
March 27, 2009

/Anne M Gussow/
Examiner, Art Unit 1643